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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 10/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/810,836	Applicant(s) BROUN, PIERRE	
	Examiner David A Lambertson	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *18-25 and 27-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,26 and 33-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of a reply, filed August 9, 2002 as Paper No. 15, to the previous Office Action. Amendment of claims 1-3, 10, 11, 15, 18, 33-36, 43, 44 and 48 have been acknowledged and entered. Amendments to the specification to comply with the requirements of 37 CFR 1.821-1.825 have been acknowledged and entered. However, applicant has not stated in the amendment that no new matter has been introduced into the specification, as required. Applicant must provide this statement accordingly.

Claims 1-18, 26 and 33-50 are ready for examination in the pending application. Any rejection of record in the previous Office Action, Paper No. 14 mailed May 9, 2002, that is not addressed in this action has been withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 10, 11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim *et al.* (*The Plant Journal* **11**(6): 1237-1251; IDS reference; see entire reference). **This rejection is maintained for reasons of record in Paper No. 13.**

Response to Arguments for 102 Rejections

Applicant's arguments filed August 9, 2002 have been fully considered but they are not found to be persuasive.

Applicant's traversal of the 102(b) rejection of claims 1, 10, 11 and 13 is not found to be persuasive. Applicant has amended the claims to contain the term "cloned", and states that support for this amendment can be found on page 10, lines 35-36. However, there does not appear to be an alternative definition for the term "cloned" in the indicated location. As such, the term "cloned" is defined with its art accepted meaning, to have copies of a DNA sequence made. As such, Kim *et al.* continues to read on the claims as amended, since the DNA as used therein must be cloned into the one-hybrid vector to be used in the assay. Therefore, the rejection of claims 1, 10, 11 and 13 by 35 U.S.C. 102(b) is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim *et al.* in view of Memelink *et al.* (WO 0046383, see entire document; henceforth the '383 publication. **This rejection is maintained for reasons of record in Paper No. 13.**

Response to Arguments for 103 Rejections

Applicant's traversal of the 103(a) rejection of claims 5-9 and 12 is also not found to be persuasive. Applicant's traversal is based on 1) the assertion that Kim *et al.* no longer teaches the elements of claims 1, 10, 11 and 13 as presented in applicant's arguments regarding the 102(b) rejection and 2) the assertion that the '383 publication does not provide "motivation to identify transcription factors using the methods of Kim *et al.* or any method at all because the transcription factor nucleotide sequences are already known" or "pre-selected".

In light of the above comments concerning the 102(b) rejection, applicant's first basis of traversal is not considered persuasive. Concerning the second basis of traversal, the examiner recites the following as an indication of an attempt to identify transcription factors in the '383 publication: on page 8, lines 5-18, the '383 publication describes a method for identifying a nucleotide sequence coding for a transcription factor, isolating it (cloning, as per applicant' amendment) and inserting it into a cell to modulate the expression of a gene involved in the biosynthesis of a metabolite. When considering the above citations, the '383 publication clearly teaches identifying transcription factor polynucleotide sequences. Therefore, applicant's assertion that all of the polynucleotide sequences in '383 are known is not accurate. Furthermore, on page 48, lines 10-22, the '383 publication teaches an embodiment of the invention as indicated above, where at least two isolated (i.e., cloned) nucleotide sequences are used, hence representing a "pool" of transcription factors. Since the '383 publication does teach the identification of polynucleotides that encode transcription factors, the ordinary skilled artisan would have been motivated to look to the teachings of Kim *et al.*, which provide a method for identifying transcription factors, to apply different techniques of transcription factor

identification in order to obtain a comprehensive analysis of all potential transcription factors. Therefore, the second basis for applicant's traversal is found unconvincing because the '383 publication does provide motivation to look to the teachings of Kim *et al.* as indicated above, hence the rejection is maintained.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1, 2, 4-14, 16, 17, 33, 35 and 37-49 are rejected under 35 U.S.C. 102(e) as being anticipated by the '383 publication. This is a new rejection not raised in the previously Office Action.

Briefly, applicant's invention is a method of detecting a transcription factor from a pool of transcription factor encoding polynucleotides (where at least one or at least two or more polynucleotides are used) by introducing the polynucleotides into a cell comprising a reporter gene operably linked to the promoter of a pathway gene, where the transcription factor encoding polynucleotides can be selected either based on structural similarity, or without regard to structural similarity. In some embodiments of the invention, more than one pathway gene is detected. In more specific embodiments of the invention, the pathway gene is a biosynthetic

pathway gene, specifically a primary or secondary metabolite-producing gene. More specifically, the genes can be terpenoid or alkaloid producing genes from plants, especially from the species *Taxus* or *Mentha*. Particular genes of interest are taxadiene synthase and limonene synthase. In some variations of the invention, the polynucleotides encoding for the transcription factor or the reporter can be expressed transiently in the cell. In some variations, the reporter gene is specifically β-glucuronidase (GUS). In some embodiments, instead of measuring the activity of the reporter, the RNA levels of the resulting transcript are measured. Finally, in at least one embodiment the invention also encompasses the deconvolution of the polynucleotide pool to identify the minimum transcription factor(s) required for gene activation.

The '383 publication teaches a method for identifying a polynucleotide sequence coding for a transcription factor, and isolating and inserting it into a host cell to modulate the expression of a gene involved in the biosynthesis of a metabolite (see for example page 8, lines 7-18), further teaching introducing at least one polynucleotide (see for example page 10, lines 11-19), but also two or more polynucleotides (see for example page 48, lines 8-22) into the cell. The polynucleotides are generally determined based on predicted structural similarity to known families of transcription factors, in particular AP2 domain containing transcription factors (see for example page 12, lines 27-32) in the '383 publication. The '383 publication further teaches that the particular biosynthesis pathway genes can be from plants (see for example page 2, lines 31-32), wherein the pathway genes are involved in the production of primary and secondary metabolites such as terpenoids and alkaloids (see for example page 10, lines 24-28 and page 28, line 26 to page 29, line 3). In particular, taxol can be produced, primarily using the plant species *Taxus*, from which it was originally isolated (see for example page 23 lines 24 and 28). The '383

patent further teaches the modulation of one or more genes using these polynucleotides (see for example page 1, line 31 to page 2, line 7), where in particular embodiments the effects on multiple genes are monitored (see for example page 21, lines 18-31). In specific examples, the polynucleotides encoding the transcription factors and a reporter gene construct fused to a promoter are transiently co-transfected into a cell where the reporter gene is GUS, and the either the enzymatic activity of GUS (see for example Example 7, page 67, lines 9-25) or the RNA levels of a target gene are monitored (see for example Example 5, page 65, lines 5-32).

New Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over the '383 publication as applied to claims 1, 2, 4-14, 16, 17, 33, 35 and 37-49 above, in view of Wildung *et al.* (*J. Biol. Chem.* **271**(16): 9201-9204, 1996, see entire document; henceforth Wildung). This is a new rejection not raised in the previous Office Action.

Applicant's invention is as stated above in the 35 U.S.C. 102(e) rejection.

The teachings of the '383 publication are described above and each aspect is applied as before. To reiterate, the '383 publication teaches the identification of transcription factors that regulate the expression of biosynthetic genes that produce primary and secondary metabolites (see for example page 8, lines 7-18 and page 10, lines 24-28 and page 28, line 26 to page 29, line 3). One of the metabolites indicated in the specification is taxol (see for example page 23 lines 24 and 28).

The '383 publication does not teach specifically the regulation of taxadiene synthase.

Wildung teaches that taxadiene synthase is the first committed step in the biosynthesis of taxol in Taxus species (see for example page 9201, first paragraph), and that taxol is an important therapeutic agent.

It would have been obvious to the ordinary skilled artisan to combine these teachings because Wildung teaches that taxadiene synthase is a gene involved in the production of taxol and the '383 publication teaches the identification of transcription factors for the regulation of metabolic genes, including those involved in the production of taxol, thus the ordinary skilled artisan would have been motivated to combine these teachings in order to improve the production of taxol, an important therapeutic agent, by identifying transcription factors useful in increasing the expression of taxadiene synthase, a gene that leads to the production of taxol, as suggested by Wildung. Absent evidence to the contrary and given the teachings of the stated prior art and the high level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 3 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over the '383 publication in view of Kim *et al.* (cited in previous 102(b) rejections above).

Applicant's invention is as stated above in the 35 U.S.C. 102(e) rejection.

The teachings of the '383 publication are described above and each aspect is applied as before. To reiterate, the '383 publication teaches the identification of transcription factors that regulate the expression of biosynthetic genes that produce primary and secondary metabolites (see for example page 8, lines 7-18 and page 10, lines 24-28 and page 28, line 26 to page 29, line 3). In a particular embodiment, the transcription factors effect transcription of genes in plants (see for example page 2, lines 31-32).

The '383 reference does not teach the selection of polynucleotides without regard to structural similarity.

Kim *et al.* teaches a method for identifying transcription factors that affect transcription of plant genes by screening a cDNA library in a "one-hybrid" system (see for example page 1237, the Abstract/Summary). The library that is being screened is designed without regard to structural similarity so as to encompass a wide range of genes in order to identify as many possible relevant transcription factors as possible.

It would have been obvious to one of ordinary skill in the art to combine the teachings of the '383 publication with those of Kim *et al.* because both teachings teach it is within the skill the skill of the art to identify transcription factors, and because Kim *et al.* teach it is within the skill of the art to screen random nucleic acid libraries for such transcription factors, the ordinary skilled artisan would have been motivated to combine these teachings in order to receive the expected benefit of being able to increase the number of potential transcription factors with the

ability to activate the expression of biosynthetic genes important for the production of primary and secondary metabolites, as suggested by Kim *et al.* Absent evidence to the contrary and given the teachings of the stated prior art and the high level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 18 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over 383 publication in view of Subramanian *et al.* (US 2002/0058249 a1; see entire document; henceforth Subramanian).

Applicant's invention is as stated above in the 35 U.S.C. 102(e) rejection.

The teachings of the '383 publication are described above and each aspect is applied as before. To reiterate the important issues regarding the specific claims being rejected, for clarity, the '383 publication teaches the identification of transcription factors that regulate the expression of biosynthetic genes that produce primary and secondary metabolites (see for example page 8, lines 7-18 and page 10, lines 24-28 and page 28, line 26 to page 29, line 3). In a particular embodiment, two or more polynucleotides (see for example page 48, lines 8-22) are examined for a desired property, the encoding of transcription factors with the ability to affect transcription of biosynthetic genes.

The '383 reference does not teach the deconvolution of pools of nucleic acids (two or more nucleic acids constituting a "pool") that give a positive response when transcriptional activity is measured.

Subramanian teaches the screening of pools of polynucleotides for a desired property, followed by deconvoluting the pool in order to identify single clones with the desired property (see for example page 14, paragraph [132]), and that this is advantageous because it increases the number of polynucleotides that can be screened, thereby increasing the chance of identifying a polynucleotide of interest.

It would have been obvious to one of ordinary skill in the art to combine the teachings of the '383 publication with those of Subramanian because both teachings teach methods for simultaneously screening multiple polynucleotides (in the form of a pool) for a desired property, thus the ordinary skilled artisan would have been motivated to combine these teachings in order to increase the number of transcription factors that are screened simultaneously for the ability to activate the expression of biosynthetic genes important for the production of primary and secondary metabolites, thereby increasing the chances of finding effective transcription factors. Absent evidence to the contrary and given the teachings of the stated prior art and the high level of skill of the ordinary skilled artisan at the time of the applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowable